Parainfectious Optic Neuritis: Manifestations in Children vs Adults

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Parainfectious Optic Neuritis: Manifestations in Children vs Adults

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Background: Parainfectious optic neuritis may appear at any age. The aim of our report was to compare the clinical manifestations and outcomes of this form of optic neuritis between children and adults.

Methods: The study sample consisted of all patients diagnosed with parainfectious optic neuritis evaluated by 2 neuro-ophthalmology services between 2005 and 2012. Data were collected retrospectively from the medical files. Findings were compared between patients aged 0–18 years and 19 years or older.

Results: Ten children (50% female) and 8 adults (50% female) met the study criteria. Mean duration of follow-up was 29.4 months (range, 2–72 months) in the pediatric group and 14.2 months (range, 5–80 months) in the adult group. Respective rates of bilateral disease were 50% and 38%, and all patients had optic disc swelling. The associated pathogen was identified in 60% of the pediatric group, mainly *Mycoplasma pneumoniae*, and 75% of the adult group, in which no microorganism predominated. The interval from the febrile illness to symptom onset was 6 days (range, 1–14 days) in the pediatric group and 19.5 days (range, 14–30 days) in the adult group. Acute disseminated encephalomyelitis (ADEM) was diagnosed in 40% (4/10) of the children and none of the adults. Final visual outcome was 20/30 or better in all patients. There was a higher frequency of bilateral disease in prepubescent vs postpubescent children.

Conclusions: Parainfectious optic neuritis is associated with a favorable visual prognosis regardless of age. Children tend to manifest visual symptoms sooner after the antecedent infectious illness and more often bilaterally and in conjunction with ADEM. The causative agent is isolated less frequently in children compared with adults.

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Optic neuritis is a major cause of visual impairment and may be due to demyelinating inflammatory and infectious etiologies (1–7). Optic neuritis associated with an infectious etiology may be due to direction invasion by the pathogen or after an infectious disease, presumably on an autoimmune basis (1). This latter setting is designated parainfectious optic neuritis.

Optic neuritis may occur at any age. The annual incidence is lower in children (0.33–1.66 per 1,000,000) than in adults (5.1 per 1,000,000) (1). The presentation also differs by age group: children more often have bilateral disease, frequently with optic disc edema (5–9). In children, after a visual illness, optic neuritis has been reported to occur in up to 66% of cases (9). Corresponding data in adults are lacking. The aim of our study was to compare the clinical manifestations, pathogenic organisms, treatment, and outcome of parainfectious optic neuritis between children and adults.

METHODS

A retrospective case series design was used. The databases of tertiary pediatric (Schneider Children's Medical Center) and adult (Kaplan Medical Center) medical center neuro-ophthalmology services were searched for all patients diagnosed with optic neuritis from January 2005 through November 2012. The main criterion for inclusion was acute onset of optic neuritis within 1 month after an infectious disease. Only patients who underwent complete evaluation including neuroimaging were included. The presence of an infectious disease was defined by the clinical history,

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laboratory findings of lymphocytosis or leukocytosis, positive serological testing in blood or cerebrospinal fluid (CSF), and positive blood or CSF culture when performed. The diagnosis of optic neuritis was based on a finding of at least one manifestation of optic nerve disease: reduced visual acuity, abnormal color vision, relative afferent pupillary defect, or visual field defect with or without optic disc edema in one or both eyes. Exclusion criteria were optic neuropathy from causes other than infection, a space-occupying lesion on brain imaging, idiopathic intracranial hypertension, and absence of evidence of infection.

The medical files and neuroimaging studies of the eligible patients were reviewed, and demographic, clinical, treatment, and outcome data were recorded. Findings were compared between patients aged 0–18 years and 19 years or older, and between prepubescent and postpubescent children, alone or combined with the adult group. The study was approved by the institutional review boards of both medical centers.

RESULTS

Twenty-four patients met the inclusion criteria, of whom 6 were later excluded because of missing hospital or follow-up data. The demographic data of the patients are shown in Tables 1 and 2. There were 10 children aged 7–16 years (mean, 12.7 years), of whom 4 were prepubescent, and 8 adults aged 19–45 years (mean, 31 years). The mean duration of follow-up was 29.4 months (range, 5–72 months) in the pediatric group and 14.2 months (range, 5–40 months) in the adult group.

The ophthalmologic findings are shown in Tables 3 and 4. Initial visual acuity was documented in 7 children, of whom 5 (71%) had acuity of 20/150 or worse, and 7 adults, of whom 6 (86%) had visual acuity of 20/40 or better. All patients had either unilateral or bilateral optic disc edema. One adult (patient 3) had a partial macular star. Systemic neurological manifestations (headache, meningitis, encephalitis) occurred in 6 children. On magnetic resonance imaging (MRI), 4 children (40%) had findings consistent with acute disseminated encephalomyelitis (ADEM) and 1 child (10%) had nonspecific white matter lesions without clinical encephalitis. In the adult group, 2 patients (25%) had nonspecific white matter lesions and 1 (12%) had lesions consistent with microangiopathic changes. None of the adults had ADEM.

Lumbar puncture demonstrated normal opening pressure in all patients. Protein and glucose levels were within normal limits in all the patients, except 2 children with meningitis, although no pathogen was identified in their CSF.

An infectious pathogen was identified by serology or culture in 6 children (60%) and 6 adults (75%) (Table 5). The main pathogen in the children's group was *Mycoplasma pneumoniae,* found in 4 of 6 patients (67%). In the adult group, there was no common pathogen.

Four children were prepubescent. Comparison of this subgroup with the postpubescent children alone (6/10) or combined with the adults (total 14 patients) yielded no differences in any of the parameters except for a higher rate of bilateral optic neuritis disease in the prepubescent subgroup (3/4, 75%).

Corticosteroid treatment was administered to 7 children and 4 adults (Tables 1 and 2). All treated children received intravenous methylprednisolone (10 mg/kg/day) for at least 3 days. Adults received either oral prednisone (2 mg/kg/day) for 2 weeks or intravenous methylprednisolone (1 g/d) for 3 days followed by oral prednisone 60 mg/d for an additional 11 days. Final visual outcome was 20/30 or better in all patients. There was no correlation between final visual outcome and whether or not steroid treatment was given. There were no instances of recurrent optic neuritis during the follow-up period.

DISCUSSION

In our study of parainfectious optic neuritis, the gender distribution was equal in the adult group and almost equal in the pediatric group. In most previous studies of optic neuritis, a female predominance has been reported and in children, the disease affected male and female patients equally before puberty and female patients more often after puberty (1,7–9). However, in these reports, cases of parainfectious optic neuritis were included in larger patient cohort studies.

In our case series, initial visual acuity tended to be worse in children but both groups had equally good visual outcomes. These results are in agreement with previous studies (1,7,10). Nevertheless, the visual field defects were milder than expected, perhaps owing to the early diagnosis due to the acute febrile disease and early and aggressive treatment (antibiotics and steroids). Interestingly, all patients had swollen discs at presentation. This finding was not mentioned in previous reports.

Our results highlight additional differences in clinical characteristics of parainfectious optic neuritis between children and adults. Time elapsed between the febrile illness and the onset of the visual symptoms was shorter in the pediatric group. This finding might be explained by a more fulminant immune response in children, manifested by the presence of bilateral optic nerve involvement and other neurological symptoms, with or without MRI abnormalities, consistent with ADEM. This may also be the reason why more children than adults experienced bilateral optic nerve involvement. This observation has been described in pediatric optic neuritis regardless of etiology (8,10,11).

In the adult group, the diagnosis of optic neuritis days to weeks after the presumed systemic infection support the theory that parainfectious optic neuritis is due to an immunologic–inflammatory reaction (1,5–11). The rare occurrence of uveitis in these cases also may be related to this reaction.

TABLE 1. Clinical data of children with parainfectious optic neuritis

Patient No.	Age, yr	Gender	Follow-up, mo	Side of ON	Preceding Infection/ Pathogen	Time From Infection to ON (days)	MRI/CT Findings at Diagnosis	MRI/CT Findings at the End of Follow-up	Treatment
1	14	F	72	Bilateral	Viral meningitis (no pathogen found)	5	Lesions in thalamus: ADEM; optic nerve enhancement	None	Steroids IV
2*	11	F	8	Bilateral	*M. pneumoniae*, febrile illness	14	2 nonspecific periventricular lesions	Not done	Steroids IV
3	14	M	40	LE	Pansinusitis	1	MRI: no lesions	Not done	Steroids IV + oral amoxicillin
4	13	F	7	RE	Sinusitis; EBV IgM	5	MRI: diffuse white matter lesions, ADEM	None	Steroids IV
5*	7	M	9	LE	Meningoencephalitis (no pathogen found)	10	MRI: multiple white matter lesions, ADEM	Some lesions disappeared or became smaller	Steroids IV + oral cefuroxime + doxycycline + acyclovir IV
6	16	F	12	Bilateral	Pneumonia, *M. pneumoniae*	5	MRI: multiple brain lesions, ADEM; optic nerve enhancement	None	Steroids IV + oral roxithromycin
7	14	M	18	RE	Nonspecific viral illness: brother had chicken pox (varicella) 7–10 days before (no pathogen found)	Unknown	No brain lesions; optic nerve enhancement	Not done	Steroids IV
8*	12	M	72	Bilateral	Nonspecific headaches, throat culture positive for *Streptococcus. pyogenes*	Unknown	No brain lesions	Not done	Oral penicillin
9	13.5	M	16	RE	Headaches, gastroenteritis; *M. pneumoniae*, IgM	5	No brain lesions	Not done	None
10*	12.5	F	40	RE	*M. pneumonia*, IgM; no febrile illness	Unknown	No brain lesions	Not done	Oral azithromycin

*Prepubescent children.

ADEM, acute disseminated encephalomyelitis; CT, computed tomography; EBV, Epstein–Barr virus; F, female; LE, left eye; M, male; MRI, magnetic resonance imaging; ON, optic neuritis; RE, right eye.

TABLE 2. Clinical data of adults with parainfectious optic neuritis

Patient No.	Age, yr	Gender	Follow-up (months)	Side of ON	Preceding Infection/ Pathogen	Time From Infection to ON (days)	MRI/CT Findings at Diagnosis	MRI/CT Findings at End of Follow-up	Treatment
1	27	M	6	Bilateral	Febrile illness, CMV IgM	28	Enlarged lateral ventricles	None	Vitamin B12 (because of deficiency)
2	23	F	5	LE	Gastroenteritis, CMV IgM	21	No abnormalities	Not done	Steroids IV and then oral
3	24	M	7.5	RE	Headache, *Coxiella burnetii*/Q fever, IgM	14	One nonspecific white matter lesion	Not done	Oral doxycycline
4	19	F	5	Bilateral	Nonspecific febrile illness (no pathogen found)	14	Optic nerve thickening, no enhancement, no brain lesions	Not done	Oral steroids
5	34	M	6	LE	Nonspecific febrile illness (no pathogen found)	28	Nonspecific white matter lesions	Not done	None
6	45	M	30	RE	Uveitis: posterior; HBV: HBcAg, HBeAb	At same time of uveitis	White matter lesions: periventricular and supraventricular (microangiopathic changes)	Not done	Oral steroids + lamivudine + steroid eye drops
7	32	F	40	RE	Fever, Toxoplasma IgM	28	No abnormalities	Not done	Oral clindamycin + pyrimethamine + sulfadiazine + leucovorin

CMV, cytomegalovirus; F, female; HBcAg, hepatitis B core antigen; HBcAb, hepatits B E antibody; HBV, hepatitis B virus; LE, left eye; M, male; ON, optic neuritis; RE, right eye.

TABLE 3. Ophthalmologic findings in children with parainfectious optic neuritis

Patient No.	At Onset					
	Optic Disc Edema	Visual Acuity		Dyschromatopsia	RAPD	VF
		RE	LE			
1	Bilateral	NA	NA	NA	NA	NA
2	Bilateral	20/150	20/50	Bilateral	RE	Binasal constriction
3	LE	20/20	FC	NA	LE	LE superior field defect
4	RE	NA = diminished	NA	NA	NA	NA
5	LE	NA	NA = diminished	NA	LE	NA
6	Bilateral	LP	20/480	Bilateral severe	RE	RE: central scotoma + superonasal constriction; LE: inferonasal constriction
7	RE	HM	20/22	Bilateral	RE	Bilateral nasal step
8	Bilateral	20/30	20/30	NA	No	Bilateral enlarged blind spot
9	RE	20/20	20/20	No	NA	RE: cecocentral scotoma
10	RE	FC	20/20	NA	RE	RE: enlarged blind spot

Patient No.	At end of Follow-up					
	Optic Disc	Visual Acuity		Dyschromatopsia	RAPD	VF
		RE	LE			
1	Bilateral temporal pallor	20/20	20/25	No	No	Generalized depression
2	Normal	20/25	20/20	No	RE mild	Normal
3	Normal	20/20	20/20	No	No	Normal
4	Normal	20/20	20/20	No	No	Normal
5	LE: mild pallor	20/20	20/30	No	No	Normal
6	Bilateral temporal pallor	20/20	20/20	No	No	Bilateral mild nasal constriction
7	Normal	20/25	20/22	No	RE: mild	RE constriction
8	Normal	20/20	20/20	No	No	Normal
9	RE: mild pallor; LE: drusen	20/20	20/20	No	No	RE: mild cecocentral scotoma
10	Normal	20/20	20/20	No	RE: trace	Normal

FC, finger counting; HM, hand motion; LE, left eye; LP, light perception; NA, not available/not checked at onset due to peer condition; RAPD, relative afferent pupillary defect; RE, right eye; VF, visual fields.

TABLE 4. Ophthalmologic findings in adults with parainfectious optic neuritis

	At Onset					
		BCVA				
Patient No.	Optic Disc Edema	RE	LE	Dyschromatopsia	RAPD	VF
1	Bilateral	20/40	20/25	No	No	Normal
2	LE	20/20	20/30	LE	LE	LE: concentric constriction
3	RE	20/20	20/20	RE	RE	RE: enlarged blind spot
4	Bilateral	20/200	20/60	Bilateral	RE	Bilateral inferior deficit
5	LE	20/40	20/40	Bilateral	LE	LE: enlarged blind spot
6	RE	20/40	20/20	RE	RE	RE: enlarged blind spot + inferior arcuate scotoma
7	RE	20/40	20/20	RE	RE	RE: enlarged blind spot

	At End of Follow-up					
		BCVA				
Patient No.	Optic disc	RE	LE	Dyschromatopsia	RAPD	VF
1	RE mild elevation	20/25	20/20	No	No	Normal
2	Normal	20/20	20/20	No	No	LE: generalized depression
3	Normal	20/20	20/20	No	No	Normal
4	Normal	20/20	20/20	No	RE	RE: enlarged blind spot
5	Normal	20/15	20/15	No	No	Bilateral inferior field loss
6	RE: disc pallor	20/30	20/20	No	No	RE: generalized depression
7	Normal	20/20	20/20	No	No	Normal

BCVA, best corrected visual acuity; LE, left eye; NA, not available/not checked due to general deteriorated condition; RAPD, relative afferent pupillary defect; RE, right eye; VF, visual fields.

TABLE 5. Comparison of children and adults with parainfectious optic neuritis in which a pathogenetic organism was identified

Characteristics	Children	Adults
Initial VA	71%: <20/40; 57%: <20/200	25%: <20; 40%: <20/200
Gender	55% female	43% female
Laterality	55% bilateral	43% bilateral
Mean age (range), yr	13 (7–17)	29 (19–45)
Site of inflammation	100% papillitis	100% papillitis
Etiology	55% positive specific serology; 4: *Mycoplasma* (36%); 1: EBV (9%); 1: *Streptococcus* A (9%)	70% positive specific serology; 2: CMV (25%); 1: Q fever (13%); 1: HBV (13%); 1: Toxoplasma (13%)
Associated encephalitis/ADEM	45%	None
MRI white matter lesions	54% (5: ADEM1 nonspecific lesions)	42% (1: microangiopathic lesions; 2: nonspecific lesions)
Time from systemic illness to ON (range), d	6 (1–14)	19 (14–30)
Treatment		
Systemic steroids	72% (all IV)	47% (IV; PO)
Systemic antibiotics	55%	29%
Vision recovery		
<20/40	None	None
At least 1 eye with ≤20/25	36%	42%

ADEM, acute disseminated encephalomyelitis; CMV-cytomegalovirus; EBV, Epstein–Barr virus; HBV, hepatitis B virus; MRI, magnetic resonance imaging; ON, optic neuritis; VA, visual acuity.

We were able to identify an infectious pathogen in 6 children (55%) and 6 adults (75%). The majority of the culture studies in the pediatric group (67%) grew *M. pneumoniae*; 2 of these cases were associated with ADEM. Among the adults with a positive culture, we did not find a common pathogen, which is consistent with the previous reports (3,4,7,11,12).

Neurological complications of *M. pneumoniae* infection in children include encephalitis and ADEM (12–21). *Mycoplasma* also has been associated with optic neuritis in children and adults (17–20). In our study, half of the children infected with *Mycoplasma* had bilateral disease, an observation described previously, especially in patients with other neurological involvement such as encephalomyelitis (16–20).

One child in our study (Table 1, patient 4) had Epstein–Barr virus–related sinusitis 5 days preceding the development of unilateral optic neuritis and ADEM. Our search of the literature yielded only one previous case report of a child with bilateral parainfectious optic neuritis related to Epstein–Barr virus infection (22). There are also reports of 4 adults, 3 of whom had concomitant systemic neurological disease (23–26).

There is no consensus regarding treatment of parainfections optic neuritis (1–8,11). In our study, children were given antibiotics and/or systemic corticosteroids more often because they had concurrent systemic disease. However, treatment was not associated with improved outcome in terms of visual acuity, visual fields, or residual optic nerve damage.

In this case series, parainfectious optic neuritis presented with optic disc swelling in 100% of the cases in both children and adults. However, we found several differences in the clinical presentation between these 2 age groups. The disease in children tends to be diagnosed earlier, presents more often bilaterally, and may be associated with ADEM. Although the causative agent was isolated less frequently in children, it tended to be consistent (usually *M. pneumoniae*). Even in the presence of negative serology and blood and CSF cultures, patients with a history and clinical presentation suggesting a preceding infection should be treated appropriately. In general, the visual prognosis is good.

We are aware of the limitations of our study. Our sample size was small, particularly the prepubescent subgroup. We attempted to exclude patients with multiple sclerosis, and none developed clinical or neuroimaging evidence of demyelinating disease. However, the follow-up period was short and brain MRI was repeated in only 5 cases. Finally, ours was a retrospective study that included potential patient selection bias and nonstandardized approaches to patient evaluation and treatment.

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